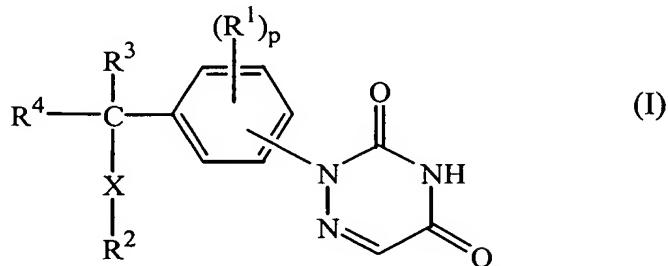


CLAIMS

1. A compound having the formula:



5 the N-oxides, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein :

p represents an integer being 0, 1, 2, 3 or 4;

X represents O, S, NR⁵ or a direct bond or-X-R² taken together may represent cyano;

10 Y represents O, S, NR⁵, or S(O)₂;

each R¹ independently represents C(=O)·Z-R¹⁴, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl, hydroxy, mercapto, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkylcarbonyloxy, aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁₋₄alkyl substituted with C(=O)·Z·R¹⁴, Het³, R⁶ or NR⁷R⁸;

15 R² represents Het¹, C₃₋₇cycloalkyl optionally substituted with C(=O)·Z·R¹⁴, C₁₋₆alkyl or C₁₋₆alkyl substituted with one or two substituents selected from C(=O)·Z·R¹⁴, hydroxy, mercapto, cyano, amino, mono- or di(C₁₋₄alkyl)amino, C₁₋₆alkyloxy optionally substituted with C(=O)·Z·R¹⁴, C₁₋₆alkylthio optionally substituted with C(=O)·Z·R¹⁴, C₁₋₆alkylsulfonyloxy, C₃₋₇cycloalkyl optionally substituted with C(=O)·Z·R¹⁴, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio;

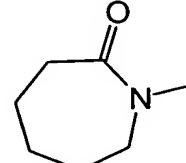
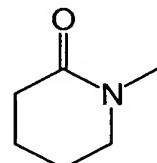
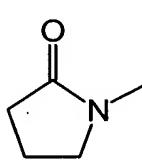
20 and if X is O, S or NR⁵, then R² may also represent aminothiocarbonyl, C₁₋₄alkylcarbonyl optionally substituted with C(=O)·Z·R¹⁴, C₁₋₄alkylthiocarbonyl optionally substituted with C(=O)·Z·R¹⁴, arylcarbonyl, arylthiocarbonyl, Het¹carbonyl or Het¹thiocarbonyl;

25 R³ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl;

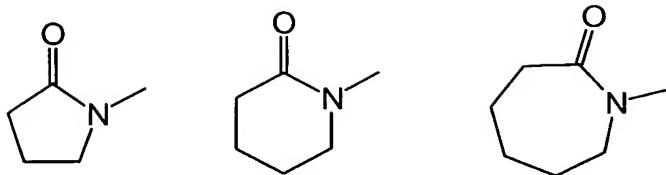
R⁴ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl; or

R³ and R⁴ taken together form a C₂₋₆alkanediyl;

R^5 represents hydrogen or C_{1-4} alkyl;
each R^6 independently represents C_{1-6} alkylsulfonyl, aminosulfonyl, piperidinylsulfonyl, mono- or di(C_{1-4} alkyl)aminosulfonyl, mono- or di(benzyl)aminosulfonyl, polyhalo C_{1-6} alkylsulfonyl, C_{1-6} alkylsulfinyl,
5 phenyl C_{1-4} alkylsulfonyl, piperazinylsulfonyl, aminopiperidinylsulfonyl, piperidinyl-aminosulfonyl, N - C_{1-4} alkyl- N -piperidinylaminosulfonyl, Y - R^{14} , mono- or di- (C_{1-4} alkyl)amino C_{1-4} alkylsulfonyl, Het^6 sulfonyl or C_{3-7} cycloalkylsulfonyl;
each R^7 and each R^8 are independently selected from hydrogen, C_{1-4} alkyl, hydroxy C_{1-4} alkyl, mercapto- C_{1-4} alkyl, dihydroxy C_{1-4} alkyl, aryl, aryl C_{1-4} alkyl,
10 C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkylcarbonyl, C_{1-4} alkyl-thiocarbonyl, arylcarbonyl, arylthiocarbonyl, Het^3 thiocarbonyl, Het^3 carbonyl, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, arylaminocarbonyl, arylaminothiocarbonyl, Het^3 aminocarbonyl, Het^3 aminothiocarbonyl, C_{3-7} cycloalkyl, pyridinyl C_{1-4} alkyl, C_{1-4} alkanediyl- $C(=O)$ - Z - R^{14} , - $C(=O)$ - Z - R^{14} , - Y - C_{1-4} alkanediyl- $C(=O)$ - Z - R^{14} , Het^3 ,
15 Het^4 and R^6 ; or R^7 and R^8 taken together with the nitrogen atom to which they are attached form a radical of formula

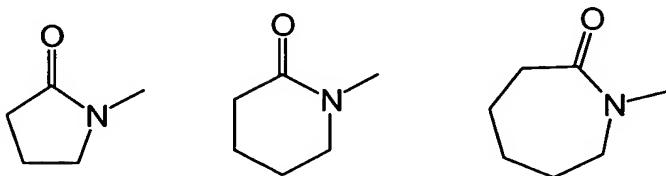


R^9 and R^{10} are each independently selected from hydrogen, C_{1-4} alkyl, hydroxy C_{1-4} alkyl, mercapto- C_{1-4} alkyl, dihydroxy C_{1-4} alkyl, phenyl,
20 phenyl C_{1-4} alkyl, C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkylcarbonyl, arylcarbonyl, Het^3 carbonyl, Het^3 thiocarbonyl, mono- or di(C_{1-4} alkyl)amino C_{1-4} alkyl, arylaminocarbonyl, arylaminothiocarbonyl, Het^3 aminocarbonyl, Het^3 aminothiocarbonyl, C_{3-7} cycloalkyl, pyridinyl C_{1-4} alkyl, C_{1-4} alkanediyl- $C(=O)$ - Z - R^{14} , - $C(=O)$ - Z - R^{14} , - Y - C_{1-4} alkanediyl- $C(=O)$ - Z - R^{14} , Het^3 ,
25 Het^4 and R^6 ; or R^9 and R^{10} taken together with the nitrogen atom to which they are attached form a radical of formula



each R¹¹ independently being selected from hydroxy, mercapto, cyano, nitro, halo, trihalomethyl, C₁₋₄alkyloxy optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkylthio optionally substituted with C(=O)-Z-R¹⁴, formyl,

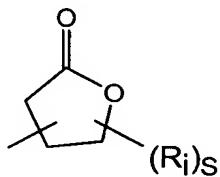
5 trihaloC₁₋₄alkylsulfonyloxy, R⁶, NR⁷R⁸, C(=O)NR¹⁵R¹⁶, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, aryl, aryloxy, arylcarbonyl, arylthiocarbonyl, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, C₃₋₇cycloalkyloxy optionally substituted with C(=O)-Z-R¹⁴, C₃₋₇cycloalkylthio optionally substituted with C(=O)-Z-R¹⁴, phthalimide-2-yl, Het³, Het⁴, C(=O)Het³, C(=O)C₁₋₄alkyl 10 optionally be substituted with one or more substituents independently selected from hydroxy, mercapto, halo and phenyl; R¹² and R¹³ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, mercapto-C₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenyl-C₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, C₁₋₄alkylthiocarbonyl, 15 arylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴ and R⁶; or R¹² and R¹³ taken together with the nitrogen atom to which they are attached form a radical of formula



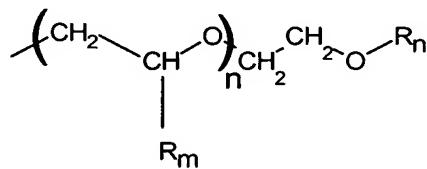
20 each R¹⁴ independently represents hydrogen; C₁₋₂₀acyl or C₁₋₂₀alkylC₁₋₂₀acyl (having a straight or branched, saturated or unsaturated hydrocarbon chain having 1 to 20 carbon atoms) optionally substituted with one or more substituents selected from hydroxy, mercapto, hydroxyC₁₋₄alkyl, mercapto-C₁₋₄alkyl, NR¹⁷R¹⁸, aryl, mono- or di-(C₁₋₄alkyl)amino, cyano and Het⁵;

C_{1-20} alkyl optionally substituted with one or more substituents selected from hydroxy, halo, mercapto, C_{1-4} alkyloxy C_{1-4} alkyloxy, mercapto C_{1-4} alkyl, $NR^{17}R^{18}$, aryl, mono- or di- $(C_{1-4}$ alkyl)amino, cyano, Het^5 , C_{1-4} alkyloxycarbonyl, aryl C_{1-4} alkyloxycarbonyl, aryl C_{1-4} alkyloxy, aryl C_{1-4} alkylthiocarbonyl,

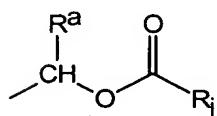
5 aryl C_{1-4} alkylthio, Het^5C_{1-4} alkyloxy, aryl C_{1-4} alkylthio, C_{3-7} cycloalkyl and Het^5C_{1-4} alkylthio; C_{3-20} alkenyl optionally substituted with phenyl; C_{3-20} alkynyl; C_{3-7} cycloalkyl optionally substituted with one or more substituents selected from hydroxy, mercapto, halo, mercapto C_{1-4} alkyl and hydroxy C_{1-4} alkyl; Het^5 or phenyl or R^{14} represents a radical having any of the following formulae:



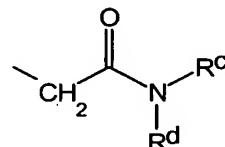
(a)



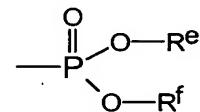
(b)



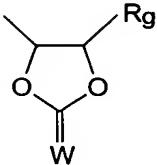
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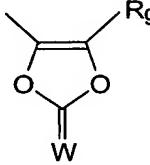
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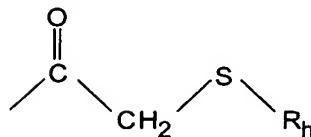
(e)



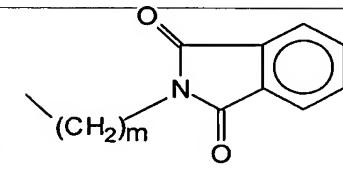
(h)



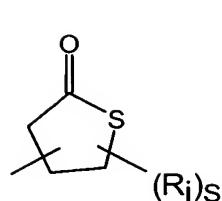
(i)



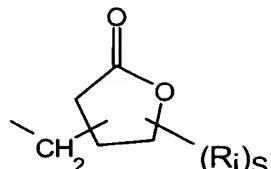
(j)



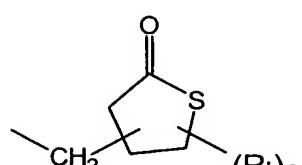
(k)



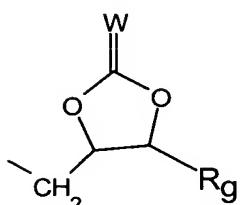
(1)



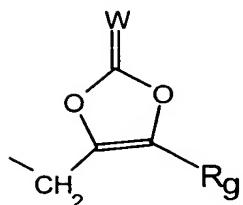
(m)



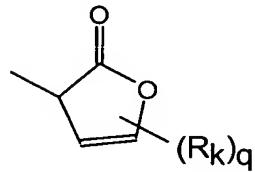
(n)



(o)



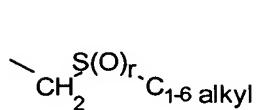
(p)



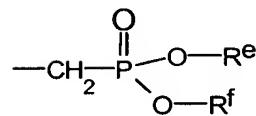
(q)



(r)



(s)



(t)

wherein m is 1 to 4, n is 0 to 5, q is 0 to 2, r is 0 to 2 and s is 0 to 4;

5 R^b is selected from hydrogen, C_{1-6} alkyl, phenyl, C_{3-7} cycloalkyl,

C₁₋₄ alkyloxyC₁₋₆alkyl and C₁₋₄ alkyl-Y-C₁₋₄alkyl;

R^a , R^c , R^d , R^e and R^f are each independently selected from hydrogen, C₁₋₆alkyl, phenyl and C₃₋₇cycloalkyl, or R^e and R^f taken together may form

-CH₂-CH₂-, -CH₂-CH₂-CH₂- or -CH₂-CH₂-CH₂-CH₂-;

10 R_g , R_h and R_k are each independently hydrogen or C_{1-4} alkyl;

R_i is selected from hydroxy, C_{3-7} cycloalkyl and C_{1-4} alkyl, or two R_i taken together may form $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$ or $-CH_2-CH_2-CH_2-CH_2-$ (thus building a spiro radical);

R_i is selected from -O-R_b; C₁₋₆alkyl optionally substituted with phenyl or

C₃₋₇cycloalkyl; phenyl; C₃₋₇cycloalkyl optionally substituted with C₁₋₄ alkyloxy and mono- or di(C₁₋₄alkyl)amino;

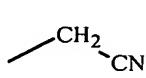
R_m is hydrogen or C₁₋₄ alkyloxy;

R_n is hydrogen, C₁₋₄alkyl, C₃₋₇cycloalkyl, phenyl or phenylC₁₋₄alkyl; and

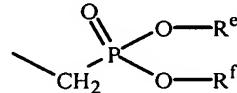
5 W represents O or S;

each Z independently represents O, S, NH, -CH₂-O- or -CH₂-S- whereby -CH₂- is attached to the carbonyl group; or

-Z-R¹⁴ taken together form a radical of formula



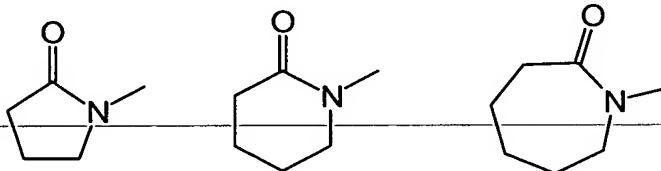
(f)



(g)

10 R¹⁵ and R¹⁶ are each independently selected from hydrogen; C₁₋₄alkyl optionally substituted with one or more substituents independently selected from hydroxy, mercapto, aryl, mono- or di(C₁₋₄alkyl) amino and pyridinyl; C₁₋₄alkyloxy; aryl; -C(=O)-Z-R¹⁴; arylcarbonyl; arylthiocarbonyl; arylaminocarbonyl; arylaminothiocarbonyl; aminocarbonylmethylene; mono- or di(C₁₋₄alkyl) aminocarbonylmethylene; Het³aminocarbonyl; Het³aminothio-carbonyl; pyridinylC₁₋₄alkyl; Het³ and R⁶; or R¹⁵ and R¹⁶ taken together with the nitrogen atom to which they are attached form a radical of formula

15



20 R¹⁷ and R¹⁸ are each independently selected from hydrogen, C₁₋₆alkyl optionally substituted with one or more substituents independently selected from hydroxy, mercapto, aryl, mono- or di(C₁₋₄alkyl) amino, C₁₋₄ alkyloxy and pyridinyl;

C₁₋₄alkyloxycarbonyl; aryl; C₁₋₄alkylcarbonyl; C₁₋₄alkylthiocarbonyl; arylcarbonyl; arylthiocarbonyl; arylaminocarbonyl; arylaminothiocarbonyl; C₃₋₇cycloalkyl;

25 C₁₋₄alkane-diyl-C(=O)-Z-C₁₋₆alkyl; -C(=O)-Z-C₁₋₆alkyl;

-Y-C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl and R⁶;

aryl represents phenyl optionally substituted with one, two or three substituents each independently selected from nitro, azido, cyano, halo, hydroxy, mercapto, C₁₋₄alkyl, C₃₋₇cycloalkyl, C₁₋₄alkyloxy, C₁₋₄alkylthio, formyl, polyhaloC₁₋₄alkyl,

5 NR⁹R¹⁰, C(=O)NR⁹R¹⁰, C(=O)-Z-R¹⁴, R⁶, -O-R⁶, phenyl, Het³, C(=O)Het³ and C₁₋₄alkyl substituted with one or more substituents each independently selected from halo, hydroxy, mercapto, C₁₋₄alkyloxy, C₁₋₄alkylthio, C(=O)-Z-R¹⁴,

-Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³ or NR⁹R¹⁰;

Het¹ represents a three-membered, four-membered, five-membered or six-

10 membered aromatic or non-aromatic, monocyclic or polycyclic heterocycle comprising one or more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus, or a fused polycyclic ring system including such heterocycle (such as for instance a fused benzoheterocycle); non-limiting examples of such heterocycles include for

15 instance pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxanyl, dithianyl,

20 trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl,

isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each

25 independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het², R¹¹ and C₁₋₄alkyl optionally substituted with one or, where possible, two or three substituents each independently selected from Het² and R¹¹;

Het² represents a three-membered, four-membered, five-membered or six-

30 membered aromatic or non-aromatic, monocyclic or polycyclic heterocycle comprising one or more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus, or a fused polycyclic

ring system including such heterocycle (such as for instance a fused benzoheterocycle); non-limiting examples of such heterocycles include for instance pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, 5 oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, 10 cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het⁴, R¹¹ and C₁₋₄alkyl optionally substituted with one or, where possible, two or three substituents 15 each independently selected from Het⁴ and R¹¹;

Het³ represents a three-membered, four-membered, five-membered or six-membered aromatic or non-aromatic monocyclic heterocycle comprising one or more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus; non-limiting examples of such heterocycles 20 include for instance pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxolanyl and tetrahydropyranyl; wherein said monocyclic heterocycles each independently may optionally be substituted with, where possible, one, two, three or four substituents each independently selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹²R¹³, 25 C(=O)-Z-R¹⁴, R⁶ and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, carbonyl C₁₋₄alkyloxy, phenyl, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, R⁶ and NR¹²R¹³;

Het⁴ represents a three-membered, four-membered, five-membered or six-membered aromatic or non-aromatic monocyclic heterocycle comprising one or 30 more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus; non-limiting examples of such heterocycles include for instance pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl,

thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and triazinyl; Het⁵ represents a three-membered, four-membered, five-membered or six-membered aromatic or non-aromatic, monocyclic or polycyclic heterocycle comprising one or more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus, or a fused polycyclic ring system including such heterocycle (such as for instance a fused benzoheterocycle); non-limiting examples of such heterocycles include for instance pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyrananyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may be substituted with, where possible, one, two, three or four substituents each independently selected from hydroxy, mercapto, carbonyl, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylthio, C₁₋₄alkylcarbonyl, piperidinyl, NR¹⁷R¹⁸, C(=O)-Z-C₁₋₆alkyl, R⁶, sulfonamido and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, C₁₋₄alkyloxy, mercapto, C₁₋₄alkylthio, phenyl, C(=O)-Z-C₁₋₆alkyl, -Y-C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl, R⁶ and NR¹⁷R¹⁸; Het⁶ represents a three-membered, four-membered, five-membered or six-membered aromatic or non-aromatic monocyclic heterocycle comprising one or more, preferably one to four, heteroatoms, preferably selected from nitrogen, oxygen, sulfur and phosphorus; non-limiting examples of such heterocycles include for instance pyrrolidinyl, piperidinyl, azaridinyl, pyrazolinyl and pyrolinyl, wherein said heterocycle may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het², R¹¹

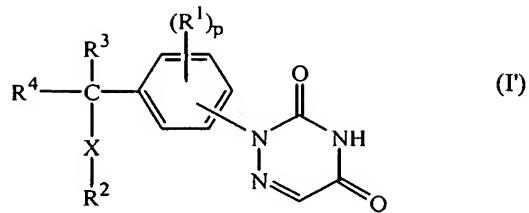
and C_{1-4} alkyl optionally substituted with one or more substituents independently selected from Het^2 and R^{11} .

provided however that

- R^2 is other than C_{1-6} alkyloxycarbonyl C_{1-6} alkyl or aminocarbonyl; and
- 5 • R^7 , R^8 , R^9 and R^{10} are other than aminocarbonyl, C_{1-4} alkylcarbonyloxy- C_{1-4} alkylcarbonyl, hydroxy C_{1-4} alkylcarbonyl, C_{1-4} alkyloxycarbonylcarbonyl, $C(=O)-O-R^{19}$, C_{1-4} alkanediyil $C(=O)-O-R^{19}$ or $-Y-C_{1-4}$ alkanediyil $C(=O)-O-R^{19}$; and
- 10 • R^{12} and R^{13} are other than C_{1-4} alkylcarbonyloxy- C_{1-4} alkylcarbonyl, hydroxy C_{1-4} alkylcarbonyl or C_{1-4} alkylcarbonylcarbonyl; and
- R^{11} is other than $C(=O)-O-R^{19}$, $Y-C_{1-4}$ alkanediyil – $C(=O)-OR^{19}$, $C(=O)NH_2$, $C(=O)NHC_{1-4}$ alkyl or $C(=O)NHC_{3-7}$ cycloalkyl; and
- 15 • R^{15} and R^{16} are other than aminocarbonyl, C_{1-4} alkylcarbonyloxy- C_{1-4} alkylcarbonyl, hydroxy C_{1-4} alkylcarbonyl or C_{1-4} alkyloxycarbonylcarbonyl; and
- aryl is other than phenyl substituted with $C(=O)-O-R^{19}$, $C(=O)NH_2$, $C(=O)NHC_{1-4}$ alkyl, $C(=O)NHC_{3-7}$ cycloalkyl and/or with C_{1-4} alkyl substituted with $C(=O)-O-R^{19}$ or $Y-C_{1-4}$ alkanediyil – $C(=O)-O-R^{14}$; and
- 20 • Het^3 is other than a monocyclic heterocycle substituted with $C(=O)-O-R^{19}$ and/or with C_{1-4} alkyl substituted with $C(=O)-O-R^{19}$ and/or $Y-C_{1-4}$ alkanediyil $C(=O)-O-R^{19}$; and
- in each of the above proviso's R^{19} is defined as hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, aminocarbonylmethylene or mono- or di(C_{1-4} alkyl)aminocarbonylmethylene; and

25 wherein the said compound having the formula (I) contains at least one $-C(=O)-Z-R^{14}$ moiety.

2. A compound according to claim 1 having the formula



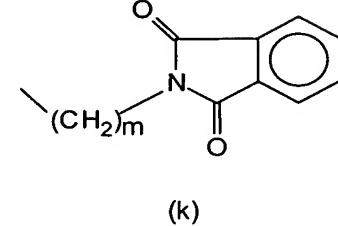
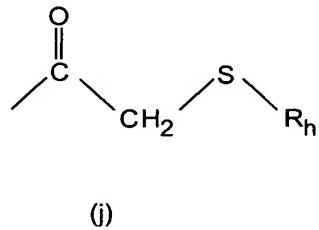
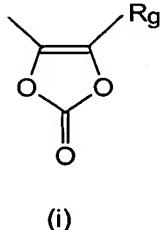
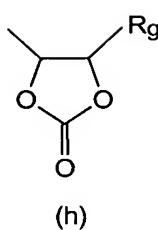
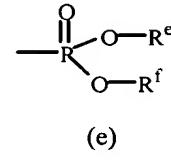
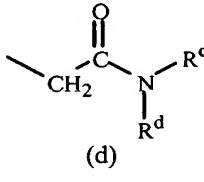
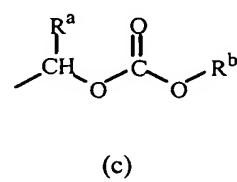
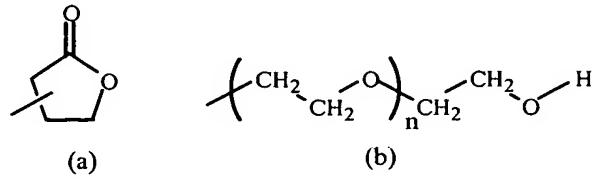
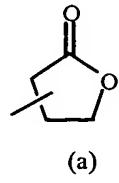
a *N*-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein :

p represents an integer being 0, 1, 2, 3 or 4;

- 5 *X* represents O, S, NR⁵ or a direct bond or-X-R² taken together may represent cyano;
- Y* represents O, S, NR⁵, or S(O)₂;
- each R¹ independently represents C(=O)-Z-R¹⁴, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl, hydroxy, mercapto, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkylcarbonyloxy,
- 10 aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁₋₄alkyl substituted with C(=O)-Z-R¹⁴, Het³, R⁶ or NR⁷R⁸;
- R² represents Het¹, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkyl or C₁₋₆alkyl substituted with one or two substituents selected from C(=O)-Z-R¹⁴, hydroxy, cyano, amino, mono- or di(C₁₋₄alkyl)amino,
- 15 C₁₋₆alkyloxy optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkylsulfonyloxy, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio; and if X is O, S or NR⁵, then R² may also represent aminothiocarbonyl, C₁₋₄alkylcarbonyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₄alkylthiocarbonyl optionally substituted with C(=O)-Z-R¹⁴ ,
- 20 arylcarbonyl, arylthiocarbonyl, Het¹carbonyl or Het¹thiocarbonyl;
- R³ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl;
- R⁴ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl; or
- R³ and R⁴ taken together form a C₂₋₆alkanediyl;
- R⁵ represents hydrogen or C₁₋₄alkyl;
- 25 each R⁶ independently represents C₁₋₆alkylsulfonyl, aminosulfonyl, mono- or di-(C₁₋₄alkyl)aminosulfonyl, mono- or di(benzyl)aminosulfonyl,

polyhaloC₁₋₆alkylsulfonyl, C₁₋₆alkylsulfinyl, phenylC₁₋₄alkylsulfonyl, piperazinylsulfonyl, aminopiperidinylsulfonyl, piperidinylaminosulfonyl, N-C₁₋₄alkyl-N-piperidinylaminosulfonyl or mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkylsulfonyl; each R⁷ and each R⁸ are independently selected from hydrogen, C₁₋₄alkyl,
5 hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, aryl, arylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, arylcarbonyl, Het³carbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiocarbonyl, Het³aminocarbonyl, Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and R⁶;
10 R⁹ and R¹⁰ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, phenylcarbonyl, Het³carbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, Het³aminocarbonyl, Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and R⁶;
15 each R¹¹ independently being selected from hydroxy, mercapto, cyano, nitro, halo, trihalomethyl, C₁₋₄alkyloxy optionally substituted with C(=O)-Z-R¹⁴, formyl, trihaloC₁₋₄alkylsulfonyloxy, R⁶, NR⁷R⁸, C(=O)NR¹⁵R¹⁶, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, aryl, aryloxy, arylcarbonyl, C₃₋₇cycloalkyl
20 optionally substituted with C(=O)-Z-R¹⁴, C₃₋₇cycloalkyloxy optionally substituted with C(=O)-Z-R¹⁴, phthalimide-2-yl, Het³, Het⁴ and C(=O)Het³;
R¹² and R¹³ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, phenylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴ and R⁶;
25 each R¹⁴ independently represents C₁₋₄ alkyl substituted with one or more substituents selected from phenyl, di- C₁₋₄alkylamino, cyano, Het¹ and C₃₋₇cycloalkyl, hydrogen, C₁₋₂₀acyl (having a straight or branched, saturated or

unsaturated hydrocarbon chain having 1 to 20 carbon atoms), C₁₋₂₀alkyl, C₃₋₇cycloalkyl, polyhaloC₁₋₂₀alkyl or a radical of formula



5 wherein n is 0 to 5 and m is 1 to 4;

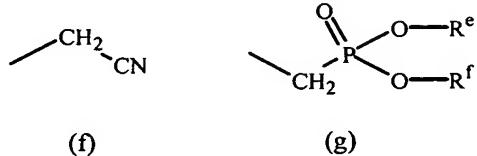
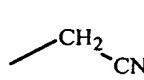
R^a, R^b, R^c, R^d, R^e and R^f are each independently hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl; or

R^e and R^f taken together may form -CH₂-CH₂-, -CH₂-CH₂-CH₂- or -CH₂-CH₂-CH₂-;

10 R_g and R_h are each independently C₁₋₄ alkyl;

each Z independently represents O, S, NH, -CH₂-O- or -CH₂-S- whereby -CH₂- is attached to the carbonyl group;

-Z-R¹⁴ taken together form a radical of formula



(f)

(g)

15 R¹⁵ and R¹⁶ are each independently selected from dihydroxyC₁₋₄alkyl, aryl, arylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, -C(=O)-Z-R¹⁴, arylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiocarbonyl, Het³aminocarbonyl, Het³aminothiocarbonyl, pyridinylC₁₋₄alkyl, Het³, Het⁴ or R⁶;

aminocarbonylmethylene or mono- or di(C₁₋₄alkyl)aminocarbonylmethylene; aryl represents phenyl optionally substituted with one, two or three substituents

each independently selected from nitro, azido, cyano, halo, hydroxy, C₁₋₄alkyl, C₃₋₇cycloalkyl, C₁₋₄alkyloxy, formyl, polyhaloC₁₋₄alkyl, NR⁹R¹⁰,

5 C(=O)NR⁹R¹⁰, C(=O)-Z-R¹⁴, R⁶, -O-R⁶, phenyl, Het³, C(=O)Het³ and C₁₋₄alkyl substituted with one or more substituents each independently selected from halo, hydroxy, C₁₋₄alkyloxy, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³ or NR⁹R¹⁰;

Het¹ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl,

10 imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, 15 isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may optionally be substituted 20 with one, or where possible, two or three substituents each independently selected from Het², R¹¹ and C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het² and R¹¹;

Het² represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl,

25 tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may optionally be

substituted with one, or where possible, two or three substituents each independently selected from Het⁴, R¹¹ and C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het⁴ and R11;

Het³ represents a monocyclic heterocycle selected from pyrrolidinyl, piperidinyl,
5 piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyran; wherein said monocyclic heterocycles each independently may optionally be substituted with, where possible, one, two, three or four substituents each independently selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹²R¹³, C(=O)-Z-R¹⁴, R⁶ and C₁₋₄alkyl substituted with one or two substituents
10 independently selected from hydroxy, C₁₋₄alkyloxy, phenyl, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, R⁶ and NR¹²R¹³;

Het⁴ represents a monocyclic heterocycle selected from pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, thieryl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and triazinyl provided however that

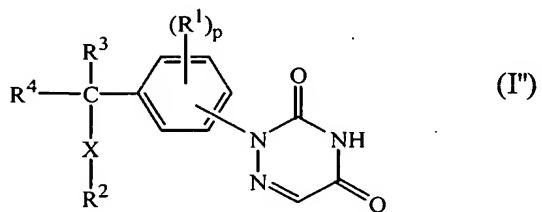
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- R² is other than C₁₋₆ alkyloxycarbonylC₁₋₆alkyl, aminocarbonyl; and
- R⁷, R⁸, R⁹ and R¹⁰ are other than aminocarbonyl, C₁₋₄alkylcarbonyloxy- C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl, C₁₋₄alkyloxycarbonylcarbonyl C(=O)-O-R¹⁴, C₁₋₄alkanediylC(=O)-O-R¹⁴ and -Y-C₁₋₄alkanediylC(=O)-O-R¹⁴; and
- 20 • R¹² and R¹³ are other than C₁₋₄alkylcarbonyloxy-C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl, C₁₋₄alkylcarbonylcabonyl; and
- R¹¹ is other than C(=O)-O-R¹⁴, Y-C₁₋₄alkanediyl – C(=O)-OR¹⁴, C(=O)NH₂, C(=O)NHC₁₋₄alkyl or C(=O)NHC₃₋₇cycloalkyl; and
- 25 • R¹⁴ is other than hydrogen, C₁₋₄alkyl, C₃₋₇cycloalkyl, aminocarbonylmethylene, mono- or di (C₁₋₄alkyl) aminocarbonylmethylene in the event Z is 0; and
- R¹⁵ and R¹⁶ are other than aminocarbonyl, C₁₋₄alkylcarbonyloxy-C₁₋₄alkylcarbonyl, hydroxy C₁₋₄alkylcarbonyl or C₁₋₄alkyloxycarbonylcarbonyl; and
- 30 • Aryl is other than phenyl substituted with C(=O)-O-R¹⁴ C(=O)NH₂, C(=O)NHC₁₋₄alkyl, C(=O)NHC₃₋₇cycloalkyl and/or with C₁₋₄alkyl substituted with C(=O)-O-R¹⁴ or Y-C₁₋₄alkanediyl – C(=O)-O-R¹⁴; and

- Het³ is other than a monocyclic heterocycle substituted with C(=O)-O-R¹⁴ and/or with C₁₋₄alkyl substituted with C(=O)-O-R¹⁴ and/or Y-C₁₋₄alkanediyl-(=O)-O-R¹⁴; and
- The said compound of formula (I) contains at least one -C(=O)-Z-R¹⁴ moiety.

5

3. A compound according to claims 1 or 2 having the formula



a N-oxide, a pharmaceutically acceptable addition salt or a stereochemically isomeric form thereof, wherein :

10 p represents an integer being 0, 1, 2, 3 or 4;
X represents O, S, NR⁵ or a direct bond or-X-R² taken together may represent cyano;
Y represents O, S, NR⁵, or S(O)₂;
each R¹ independently represents C(=O)-Z-R¹⁴, C₁₋₆alkyl, halo, polyhaloC₁₋₆alkyl, hydroxy, mercapto, C₁₋₆alkyloxy, C₁₋₆alkylthio, C₁₋₆alkylcarbonyloxy, aryl, cyano, nitro, Het³, R⁶, NR⁷R⁸ or C₁₋₄alkyl substituted with C(=O)-Z-R¹⁴, Het³, R⁶ or NR⁷R⁸;
15 R² represents Het¹, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkyl or C₁₋₆alkyl substituted with one or two substituents selected from C(=O)-Z-R¹⁴, hydroxy, cyano, amino, mono- or di(C₁₋₄alkyl)amino, C₁₋₆alkyloxy optionally substituted with C(=O)-Z-R¹⁴, C₁₋₆alkylsulfonyloxy, C₃₋₇cycloalkyl optionally substituted with C(=O)-Z-R¹⁴, aryl, aryloxy, arylthio, Het¹, Het¹oxy and Het¹thio; and if X is O, S or NR⁵, then R² may also represent aminothiocarbonyl, C₁₋₄alkylcarbonyl optionally substituted with C(=O)-Z-R¹⁴, C₁₋₄alkylthiocarbonyl optionally substituted with C(=O)-Z-R¹⁴, arylcarbonyl, arylthiocarbonyl, Het¹carbonyl or Het¹thiocarbonyl;
20 R³ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl;
R⁴ represents hydrogen, C₁₋₆alkyl or C₃₋₇cycloalkyl; or

R³ and R⁴ taken together form a C₂₋₆alkanediyl;

R⁵represents hydrogen or C₁₋₄alkyl;

each R⁶ independently represents C₁₋₆alkylsulfonyl, aminosulfonyl,

piperidinylsulfonyl, mono- or di(C₁₋₄alkyl)aminosulfonyl, mono- or

5 di(benzyl)aminosulfonyl, polyhaloC₁₋₆alkylsulfonyl, C₁₋₆alkylsulfinyl,

phenylC₁₋₄alkylsulfonyl, piperazinylsulfonyl, aminopiperidinylsulfonyl,

piperidinylaminosulfonyl,

N-C₁₋₄alkyl-N-piperidinylaminosulfonyl or mono- or

di(C₁₋₄alkyl)aminoC₁₋₄alkylsulfonyl;

10 each R⁷ and each R⁸ are independently selected from hydrogen, C₁₋₄alkyl,

hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, aryl, arylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl,

C₁₋₄alkylcarbonyl, arylcarbonyl, Het³carbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋

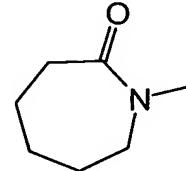
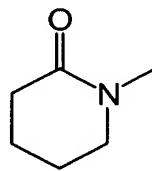
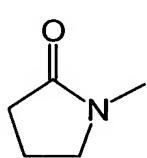
4alkyl, arylaminocarbonyl, arylaminothiocarbonyl, Het³aminocarbonyl,

Het³aminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-

15 C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and

R⁶; or R⁷ and R⁸ taken together with the nitrogen atom to which they are

attached form a radical of formula



20

R⁹ and R¹⁰ are each independently selected from hydrogen, C₁₋₄alkyl,

hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl,

C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, phenylcarbonyl, Het³carbonyl, mono-

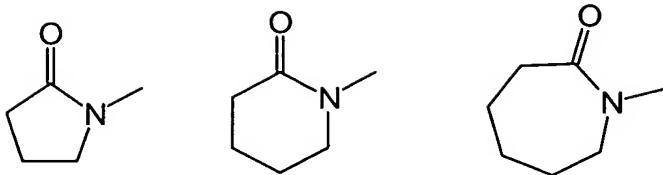
or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl,

phenylaminothiocarbonyl, Het³aminocarbonyl, Het³aminothiocarbonyl, C₃₋

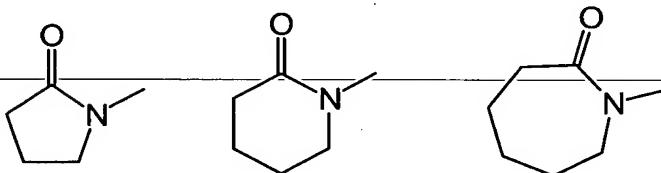
7cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, -C(=O)-Z-R¹⁴, -Y-

C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³, Het⁴ and R⁶; or R⁹ and R¹⁰ taken together

with the nitrogen atom to which they are attached form a radical of formula

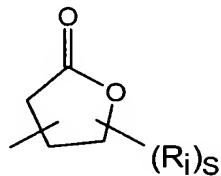


each R^{11} independently being selected from hydroxy, mercapto, cyano, nitro,
5 halo, trihalomethyl, C_{1-4} alkyloxy optionally substituted with $C(=O)-Z-R^{14}$,
formyl, trihalo C_{1-4} alkylsulfonyloxy, R^6 , NR^7R^8 , $C(=O)NR^{15}R^{16}$, $-C(=O)-Z-R^{14}$, -
 $Y-C_{1-4}$ alkanediyl- $C(=O)-Z-R^{14}$, aryl, aryloxy, arylcarbonyl, C_{3-7} cycloalkyl
optionally substituted with $C(=O)-Z-R^{14}$, C_{3-7} cycloalkyloxy optionally
substituted with $C(=O)-Z-R^{14}$, phthalimide-2-yl, Het^3 , Het^4 and $C(=O)Het^3$;
10 R^{12} and R^{13} are each independently selected from hydrogen, C_{1-4} alkyl,
hydroxy C_{1-4} alkyl, dihydroxy C_{1-4} alkyl, phenyl, phenyl C_{1-4} alkyl,
 C_{1-4} alkyloxy C_{1-4} alkyl, C_{1-4} alkylcarbonyl, phenylcarbonyl, mono- or
di(C_{1-4} alkyl)amino C_{1-4} alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl,
 C_{3-7} cycloalkyl, pyridinyl C_{1-4} alkyl, C_{1-4} alkanediyl- $C(=O)-Z-R^{14}$, $-C(=O)-Z-R^{14}$, -
15 $Y-C_{1-4}$ alkanediyl- $C(=O)-Z-R^{14}$ and R^6 ; or R^{12} and R^{13} taken together with the
nitrogen atom to which they are attached form a radical of formula

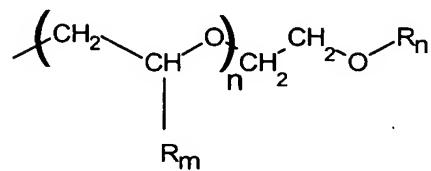


20 each R^{14} independently represents hydrogen, C_{1-20} acyl (having a straight or
branched, saturated or unsaturated hydrocarbon chain having 1 to 20
carbon atoms), C_{1-20} alkyl, C_{3-20} alkenyl optionally substituted with phenyl,
 C_{3-20} alkynyl, C_{3-7} cycloalkyl, polyhalo C_{1-20} alkyl, Het^5 , phenyl or C_{1-20} alkyl
substituted with one or more substituents selected from hydroxy, $NR^{17}R^{18}$,
25 phenyl, mono- or di- $(C_{1-4}$ alkyl)amino, cyano, Het^5 , C_{1-4} alkyloxycarbonyl,

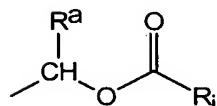
phenyl C₁₋₄ alkyloxycarbonyl and C₃₋₇ cycloalkyl, or R¹⁴ represents a radical of formula



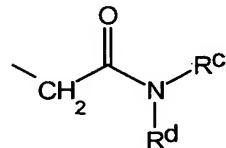
(a)



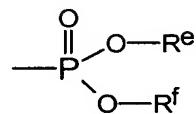
(b)



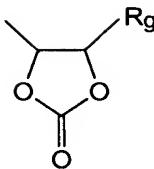
(c)



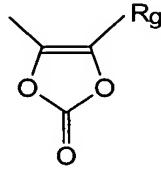
(d)



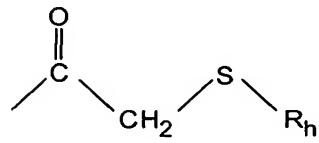
(e)



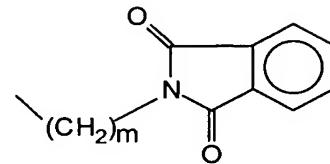
(h)



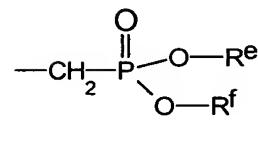
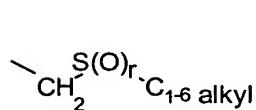
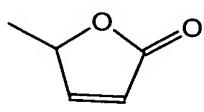
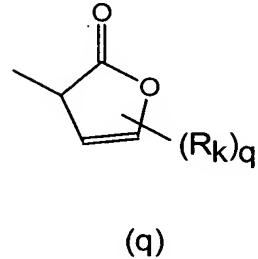
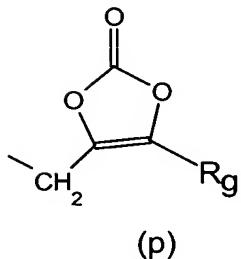
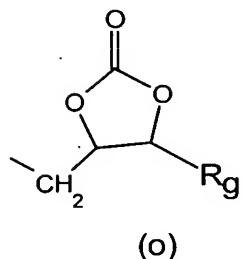
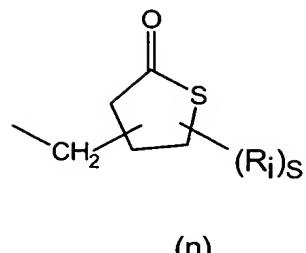
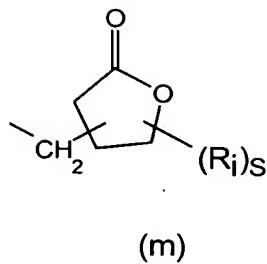
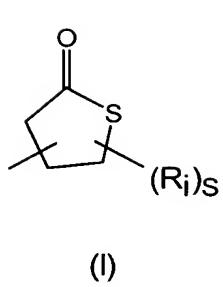
(i)



(j)



(k)



wherein m is 1 to 4, n is 0 to 5, q is 0 to 2, r is 0 to 2 and s is 0 to 4;

R^a, R^b, R^c, R^d, R^e and R^f are each independently hydrogen, C₁₋₆alkyl, phenyl or

5 C₃₋₇cycloalkyl; or

R^e and R^f taken together may form -CH₂-CH₂-, -CH₂-CH₂-CH₂- or -CH₂-CH₂-CH₂-;

R_g, R_h and R_k are each independently hydrogen or C₁₋₄ alkyl;

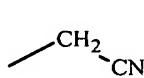
R_i is C₁₋₄alkyl;

10 R_j is -O-R_b, C₁₋₆alkyl, phenyl or C₃₋₇cycloalkyl optionally substituted with C₁₋₄ alkyloxy;

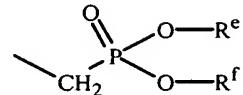
where R_m is hydrogen or C₁₋₄ alkyloxy and R_n is hydrogen, C₁₋₄alkyl, C₃₋₇cycloalkyl, phenyl or phenylC₁₋₄alkyl

each Z independently represents O, S, NH, -CH₂-O- or -CH₂-S- whereby -CH₂- is attached to the carbonyl group; or

-Z-R¹⁴ taken together form a radical of formula



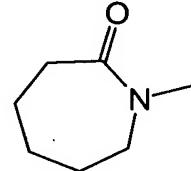
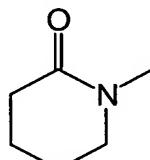
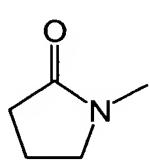
(f)



(g)

5 R¹⁵ and R¹⁶ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, aryl, arylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, -C(=O)-Z-R¹⁴, arylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, arylaminocarbonyl, arylaminothiocarbonyl, aminocarbonylmethylene, mono- or di(C₁₋₄alkyl) aminocarbonylmethylene, Het³aminocarbonyl, Het³aminothiocarbonyl,

10 pyridinylC₁₋₄alkyl, Het³ or R⁶; or R¹⁵ and R¹⁶ taken together with the nitrogen atom to which they are attached form a radical of formula



15

R¹⁷ and R¹⁸ are each independently selected from hydrogen, C₁₋₄alkyl, hydroxyC₁₋₄alkyl, dihydroxyC₁₋₄alkyl, phenyl, phenylC₁₋₄alkyl, C₁₋₄alkyloxyC₁₋₄alkyl, C₁₋₄alkylcarbonyl, phenylcarbonyl, mono- or di(C₁₋₄alkyl)aminoC₁₋₄alkyl, phenylaminocarbonyl, phenylaminothiocarbonyl, C₃₋₇cycloalkyl, pyridinylC₁₋₄alkyl, C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl, -C(=O)-Z-C₁₋₆alkyl, -Y-C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl and R⁶;

20 aryl represents phenyl optionally substituted with one, two or three substituents each independently selected from nitro, azido, cyano, halo, hydroxy, C₁₋₄alkyl, C₃₋₇cycloalkyl, C₁₋₄alkyloxy, formyl, polyhaloC₁₋₄alkyl, NR⁹R¹⁰, C(=O)NR⁹R¹⁰, C(=O)-Z-R¹⁴, R⁶, -O-R⁶, phenyl, Het³, C(=O)Het³ and C₁₋₄alkyl

25 substituted with one or more substituents each independently selected from

halo, hydroxy, C₁₋₄alkyloxy, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, Het³ or NR⁹R¹⁰;

Het¹ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, 5 tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, 10 benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het², R¹¹ and 15 C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het² and R¹¹;

Het² represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, 20 tetrahydrofuranyl, thienyl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, isobenzofuranyl, 25 benzothiazolyl, benzoxazolyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het⁴, R¹¹ and C₁₋₄alkyl optionally substituted with one or two substituents independently selected from Het⁴ and R¹¹;

Het³ represents a monocyclic heterocycle selected from pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl and tetrahydropyranyl; wherein said monocyclic heterocycles each independently may optionally be substituted with, where possible, one, two, three or four substituents each independently

5 selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹²R¹³, C(=O)-Z-R¹⁴, R⁶ and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, C₁₋₄alkyloxy, phenyl, C(=O)-Z-R¹⁴, -Y-C₁₋₄alkanediyl-C(=O)-Z-R¹⁴, R⁶ and NR¹²R¹³;

10 Het⁴ represents a monocyclic heterocycle selected from pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, thieryl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and triazinyl;

15 Het⁵ represents a heterocycle selected from pyrrolyl, pyrrolinyl, imidazolyl, imidazolinyl, pyrazolyl, pyrazolinyl, triazolyl, tetrazolyl, furanyl, tetrahydrofuran, thieryl, thiolanyl, dioxolanyl, oxazolyl, oxazolinyl, isoxazolyl, thiazolyl, thiazolinyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, tetrahydropyranyl, dioxanyl, dithianyl, trithianyl, triazinyl, benzothienyl, isobenzothienyl, benzofuranyl, 20 isobenzofuranyl, benzothiazolyl, benzoxazolyl, benzodioxanyl, indolyl, isoindolyl, indolinyl, purinyl, 1*H*-pyrazolo[3,4-d]pyrimidinyl, benzimidazolyl, quinolyl, isoquinolyl, cinnolinyl, phtalazinyl, quinazolinyl, quinoxalinyl, thiazolopyridinyl, oxazolopyridinyl and imidazo[2,1-b]thiazolyl; wherein said heterocycles each independently may be substituted with, where possible,

25 one, two, three or four substituents each independently selected from hydroxy, C₁₋₄alkyl, C₁₋₄alkyloxy, C₁₋₄alkylcarbonyl, piperidinyl, NR¹⁷R¹⁸, C(=O)-Z-C₁₋₆alkyl, R⁶, sulfonamido and C₁₋₄alkyl substituted with one or two substituents independently selected from hydroxy, C₁₋₄alkyloxy, phenyl, C(=O)-Z-C₁₋₆alkyl, -Y-C₁₋₄alkanediyl-C(=O)-Z-C₁₋₆alkyl, R⁶ and NR¹⁷R¹⁸ ; provided however that

- R² is other than C₁₋₆ alkyloxycarbonylC₁₋₆alkyl or aminocarbonyl; and

- R^7 , R^8 , R^9 and R^{10} are other than aminocarbonyl, $C_{1-4}alkylcarbonyloxy-C_{1-4}alkylcarbonyl$, hydroxy $C_{1-4}alkylcarbonyl$, $C_{1-4}alkyloxycarbonylcarbonyl$, $C(=O)-O-R^{19}$, $C_{1-4}alkanediylC(=O)-O-R^{19}$ or $-Y-C_{1-4}alkanediylC(=O)-O-R^{19}$; and
- 5 • R^{12} and R^{13} are other than $C_{1-4}alkylcarbonyloxy-C_{1-4}alkylcarbonyl$, hydroxy $C_{1-4}alkylcarbonyl$ or $C_{1-4}alkylcarbonylcarbonyl$; and
- R^{11} is other than $C(=O)-O-R^{19}$, $Y-C_{1-4}alkanediyl-C(=O)-OR^{19}$, $C(=O)NH_2$, $C(=O)NHC_{1-4}alkyl$ or $C(=O)NHC_{3-7}cycloalkyl$; and
- R^{15} and R^{16} are other than aminocarbonyl, $C_{1-4}alkylcarbonyloxy-C_{1-4}alkylcarbonyl$, hydroxy $C_{1-4}alkylcarbonyl$ or $C_{1-4}alkyloxycarbonylcarbonyl$; and
- 10 • aryl is other than phenyl substituted with $C(=O)-O-R^{19}$, $C(=O)NH_2$, $C(=O)NHC_{1-4}alkyl$, $C(=O)NHC_{3-7}cycloalkyl$ and/or with $C_{1-4}alkyl$ substituted with $C(=O)-O-R^{19}$ or $Y-C_{1-4}alkanediyl-C(=O)-O-R^{14}$; and
- 15 • Het^3 is other than a monocyclic heterocycle substituted with $C(=O)-O-R^{19}$ and/or with $C_{1-4}alkyl$ substituted with $C(=O)-O-R^{19}$ and/or $Y-C_{1-4}alkanediyl-C(=O)-O-R^{19}$; and
- in each of the above proviso's R^{19} is defined as hydrogen, $C_{1-4}alkyl$, $C_{3-7}cycloalkyl$, aminocarbonylmethylene or mono- or di($C_{1-4}alkyl$)aminocarbonylmethylene; and
- 20 • the said compound of formula (I) contains at least one $-C(=O)-Z-R^{14}$ moiety.

- 4. A compound according to any of claims 1 to 3 wherein the 6-azauracil moiety is in the para position relative to the carbon atom bearing the $-X-R^2$, R^3 and R^4 substituents.
- 25 5. A compound according to any of claims 1 to 4 wherein R^2 is a monocyclic heterocycle selected from pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, furanyl, thienyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, thiadiazolyl, oxadiazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyranyl, pyridazinyl and

triazinyl, wherein said monocyclic heterocycles each independently may optionally be substituted with one, or where possible, two or three substituents each independently selected from Het^2 , R^{11} and $\text{C}_{1-4}\text{alkyl}$ optionally substituted with Het^2 or R^{11} .

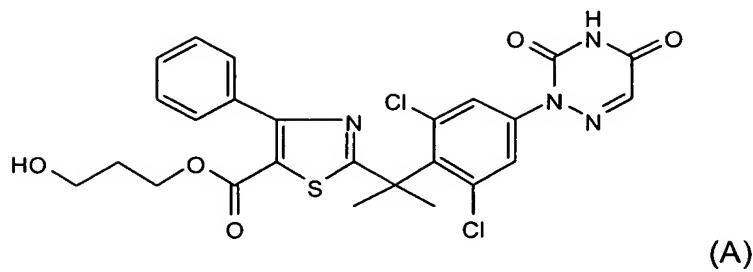
5 6. A compound according to any of claims 1 to 5 wherein R³ and R⁴ are both methyl and -X-R² is Het¹.

10 7. A compound according to any of claims 1 to 6 wherein p is 1 or 2 and each R¹ is chloro.

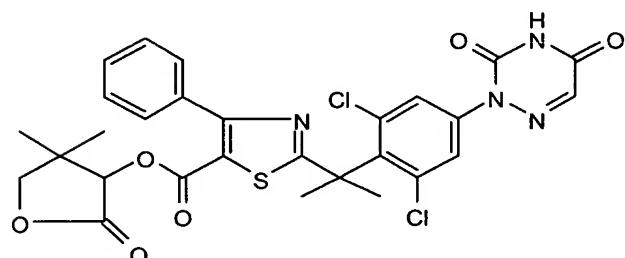
15 8. A compound according to any of claims 1 to 7 wherein R³ and R⁴ are both methyl, -X-R² is optionally substituted 2-thiazolyl or 3-oxadiazolyl, the 6-azauracil moiety is in the para position relative to the carbon atom bearing the -X-R², R³ and R⁴ substituents, and p is 2 whereby both R¹ substituents are chloro positioned ortho relative to the carbon atom bearing the -X-R², R³ and R⁴ substituents.

20 9. A compound according to claim 8 wherein X-R² is di-substituted with phenyl and either (i) R¹¹ where R¹¹ is a group of formula -C(=O)-Z-R¹⁴ in which Z is O and R¹⁴ is C₁₋₂₀alkyl substituted with hydroxy or with Het⁵ where Het⁵ is piperazinyl substituted with Het⁶sulfonyl, or R¹⁴ is a radical of formula (a) in which R_j is C₁₋₆alkyl and s is 2, or (ii) C₁₋₄alkyl substituted with R¹¹ where R¹¹ is a group of formula -C(=O)-Z-R¹⁴ in which Z is O and R¹⁴ is a radical of formula (a) in which R_j is C₁₋₆alkyl and s is 2.

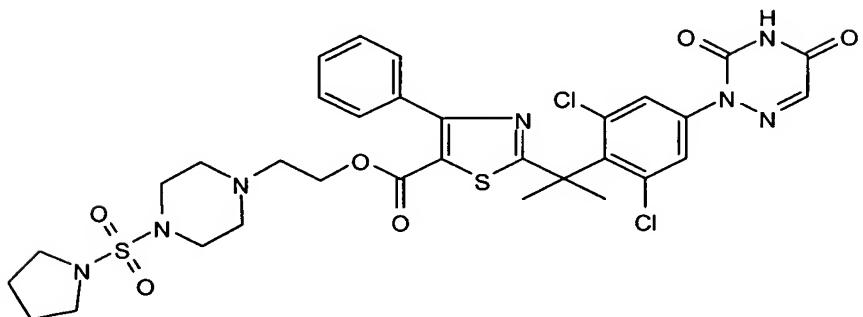
25 10. A compound according to claim 1 selected from those of formulae (A), (B), (C) and (D) below:-



(A)

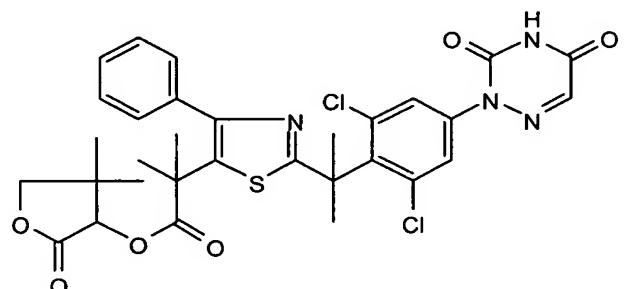


(B)



5

(C)



(D)

11. A composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound according to any of claims 1 to 10.

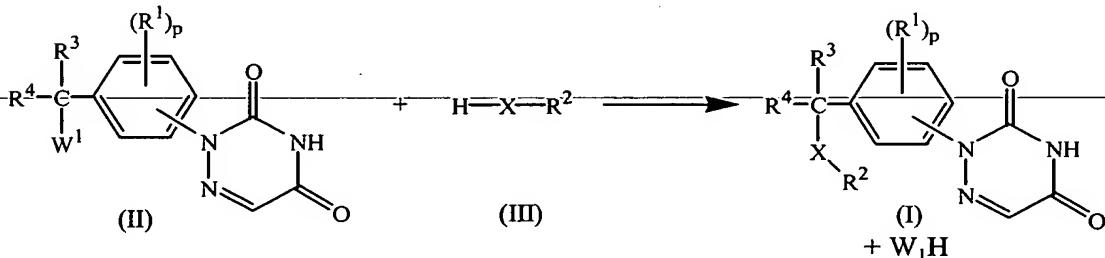
5 12. A process for preparing a composition as claimed in claim 11, wherein a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound according to any of claims 1 to 10.

10 13. A compound as claimed in any one of claims 1 to 10 for use as a medicine.

14. Use of a compound according to any of claims 1 to 10 in the manufacture of a medicament for treating eosinophil-dependent inflammatory diseases.

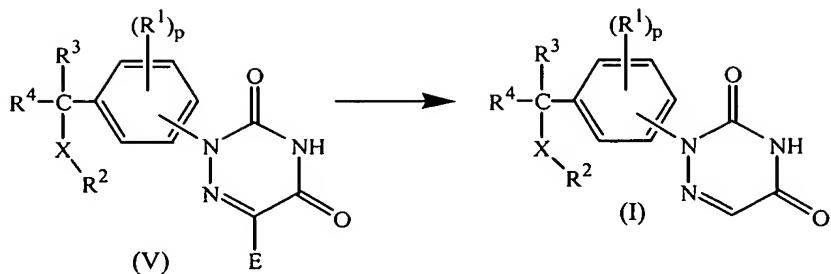
15 15. A process for preparing a compound as claimed in claim 1, comprising the step of

20 a) reacting an intermediate of formula (II) wherein W^1 is a suitable leaving group with an appropriate reagent of formula (III) optionally in a reaction-inert solvent and optionally in the presence of a base at a temperature ranging between -70°C and reflux temperature;



wherein R^1 R^2 , R^3 , R^4 , p and X are as defined in claim 1 or;

b) eliminating the group E of a triazinedione of formula (V)



wherein E is an appropriate electron attracting group and R¹, R², R³, R⁴, X and p are as defined in claim 1; and, if desired, converting compounds of formula (I) into each other following art-known transformations, and further, if desired,

5 converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali; or converting the base addition salt into the free acid by treatment with acid; and also, if
10 desired, preparing stereochemically isomeric forms or *N*-oxide forms thereof.

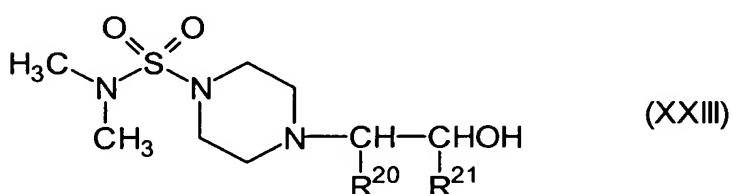
16. A process of marking a receptor comprising the steps of

15 a) radiolabelling a compound as defined in claim 1;
b) administering said radiolabelled compound to biological material,
c) detecting the emissions from the radiolabelled compound.

17 A process of imaging an organ, characterized by, administering a sufficient amount of a radiolabelled compound of formula (I) in an appropriate composition, and detecting the emissions from the radioactive compound.

20

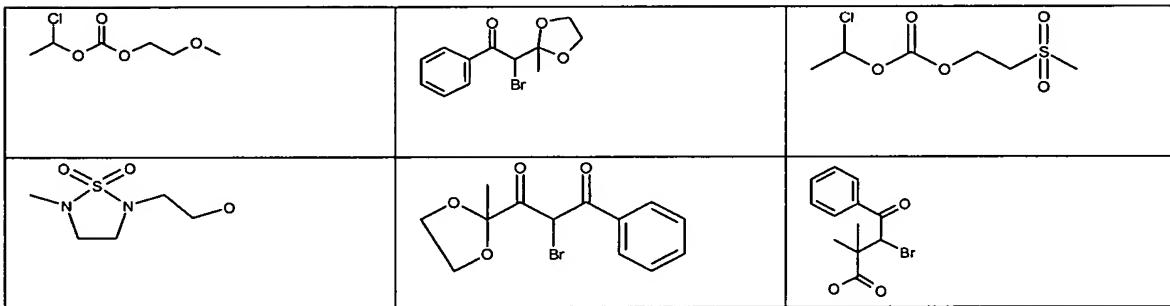
18. A compound of formula



wherein R²⁰ and R²¹ are each independently selected from hydrogen or C₁₋₂₀ alkyl or R²⁰ and R²¹ taken together with the carbon atom to which they are attached form a cycloalkyl radical.

5 19. Use of a compound of claim 18 for preparing a compound of claim 1
wherein Het⁵ represents a sulfonamido substituted piperazine.

20. A compound having any of the following formulae:



10 21. Use of a compound of claim 20 as an intermediate for preparing a compound of claim 1.